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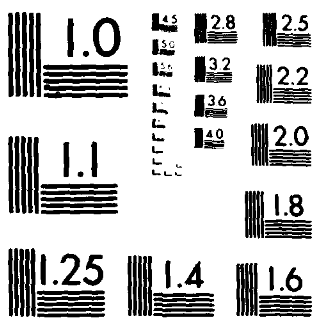

MICROCOPY RESOLUTION TEST CHART

THE EFFECT OF EXPERIMENTALLY INDUCED VIRAL INFECTION ON PHYSICAL PERFORMANCE CAPACITY

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WILLIAM L. DANIELS, ~~CPT, MS, Ph.D.~~, JAMES E. WRIGHT, ~~CPT, MS, Ph.D.~~
JOSEPH J. KNAPIK, ~~CPT, M.S.~~, JAMES A. VOGEL, ~~Ph.D.~~
GORAN FRIMAN, M.D. and WILLIAM R. BEISEL, M.D.
US ARMY RESEARCH INSTITUTE OF
ENVIRONMENTAL MEDICINE
NATICK, MA 01760
US ARMY MEDICAL RESEARCH INSTITUTE OF
INFECTIOUS DISEASES
FORT DETRICK, MARYLAND 21701

I. Introduction

The purpose of this study was to investigate the effect of a viral infection upon the individual soldier's performance capabilities. Sandfly fever was induced for this study, not because of any threat which sandfly fever may potentially carry, but because it is an appropriate disease model for a viral infection. Sandfly fever, known medically as Phlebotomus or Papatasi fever, is a self-limiting febrile illness which is transmitted by biting insects of the genus Phlebotomus. Although this illness is not serious clinically, it does have a tendency toward explosive outbreaks in large groups of susceptible individuals after short periods of exposure and thus has some potential for hazard to military operations in certain parts of the world. However, the reason for its use in this study is that it is a well understood, limited, viral illness which is suitable for study as a model infection.

The disease is characterized by the sudden onset of flu-like symptoms. These include headache, generalized malaise, photophobia and aching in the muscles and joints. The most common clinical feature is leukopenia, which is a decrease in the white blood cell count. Anorexia, nausea and vomiting may also be associated with ill defined abdominal distress. The disease has a very predictable clinical course with no sequalae or complications (1).

The purpose of this study was to evaluate the ability of soldiers to perform physical exercise during the febrile and early convalescent periods of an acute infectious disease. The effect of the disease on measurements used to assess an individual's level of physical conditioning were also determined.

II. Methodology

For this study, 9 subjects (7 experimentals, 2 controls) volunteered to undergo a series of tests before, during and after an experimentally induced episode of sandfly fever. The 2 control subjects were sham-inoculated with isotonic saline. The 7 experimental subjects were inoculated with plasma containing the sandfly fever virus. This plasma had been obtained, on the first day of illness, from a previous human volunteer. The overall experimental schedule for the study is outlined in Table 1.

Test subjects were divided into two groups for initial testing. While one group performed the aerobic test procedures, the second group performed the muscle strength tests. The morning of days -4 and -2 served as an introductory period for the test subjects. During this time, they were familiarized with the tests that they were to undergo.

On the afternoon of days -4 and -2 subjects began testing. The aerobic portion consisted of three types of procedures:

1) resting measurements
2) submaximal walking
3) maximal oxygen uptake ($\dot{V}O_2max$) test

1. Resting measurements

At the beginning of each aerobic exercise session, subjects underwent resting measurements of heart rate (12 lead ECG), blood pressure and rectal temperature. In addition, all subjects performed a pulmonary function test. Weight and skin fold measures were taken for estimation of % body fat.

2. Submaximal walking

After the resting measurements, subjects began walking on a motor-driven treadmill at a speed of 3 mph and 0% grade. Every 3 minutes the grade was increased by 3% up to a maximum work load of 15% grade. During the last minute at each work load, heart rate,

Table 1: Experimental Schedule

Day of Week	Study Day	Testing Procedure: Aerobic	Testing Procedure: Strength
Friday	-7	Screening Physical	-
Monday	-4	AM Introduction of Procedures to Group A PM Sub-max Walking Group A	Group B Static & Dynamic
Tuesday	-3	Running $\dot{V}O_2max$ on Group A	Group B Hand-grip
Wednesday	-2	AM Introduction of Procedure to Group B PM Sub-max Walking Group B	Group A Static & Dynamic
Thursday	-1	Running $\dot{V}O_2max$ on Group B	Group A Hand-grip
Friday	0	Inoculation with Plasma or Saline 0800 hours	-
Sunday	2	Hospitalization 1200 hours	-
Monday	3	PM Sub-max Walking for Febrile S's	AM Static Dynamic & Handgrip on Febrile S's
Tuesday	4	PM Sub-max Walking for Remaining S's	AM Static Dynamic & Handgrip on Remaining S's
Thursday	6	AM Sub-max Walking for S's Febrile on Day 3. PM $\dot{V}O_2max$ run	AM Static Dynamic Hand-grip on S's Day 3
Friday	7	AM Sub-max Walking on Remaining S's PM $\dot{V}O_2max$ run	AM Static Dynamic & Handgrip on Remaining S's
		Hospital Discharge 1600 hours	

blood pressure, RPE, rectal temperature and oxygen consumption were measured. Rating of perceived exertion (RPE) is a measure of perception of effort and is a valid predictor for the point at which an individual will discontinue work (2).

3. Maximal oxygen uptake ($\dot{V}O_2$max) test

During the pre- and post-fever exercise session, the subject performed a $\dot{V}O_2$max determination. Initially, all subjects began running on the treadmill at a speed of 6 mph and 0% grade for 6 minutes. Following a 5-10 minute rest period, two to four additional runs were performed, each interrupted by a rest period. Work load was increased by adjusting speed and/or grade. During the last minute of each work load expired air was collected and analyzed. A plateau in oxygen consumption was defined as $\dot{V}O_2$max.

Muscle strength capacities were assessed by both static and dynamic strength and endurance tests.

Maximal static strength

Maximal static strength of three muscle groups were measured by a device designed in this lab (3). The muscle groups tested were: upper torso, trunk extensors and legs. Two 3-4 second maximal isometric contractions were performed for each muscle group with a one minute rest between contractions. Forces were registered on electronic force transducers (BLD Model C2M1) and through digital transducer indicators (BLH Model 450A) were input displayed and recorded in a DECLAB 11/03 minicomputer which analyzed the force curves at 0.01/sec intervals.

Strength of the upper torso group was assessed with the subject securely fastened in a sitting position with a lap belt. The upper arms were positioned parallel to the floor with the elbows at a 90° angle. The hands grasped an overhead bar that is attached by a cable to the force transducer.

Strength of the leg extensors was assessed with the subject seated as above with the knees bent at 90°, the arch of the feet pushing against a bar attached by a cable to the transducer.

Strength of the trunk extensors was assessed with the subject in a standing position with the shoulders strapped to a bar which was connected to a transducer. The subject flexed back against the shoulder harness while driving the pelvic girdle against a stabilizing plate.

Isometric grip strength was measured with a handgrip ergometer which was adjusted for each subject so as to allow maximal grip output. Subjects exerted maximal grip strength for 3-5 seconds which was transferred through a turn-buckle to a force transducer and into the DECLAB 11/03 minicomputer. Static handgrip strength endurance time at 40% maximal force was assessed using the same apparatus.

Dynamic muscle strength

Maximal dynamic strength and power of the elbow-flexors and knee extensors was assessed utilizing isokinetic measuring equipment (Cybex Div., Lumex Corp., Bayshore, NY). For both the arm and leg measurements, the subject was seated and fastened by arm, leg and shoulder restraints into a heavy well-padded wooden chair which was in turn securely coupled to the isokinetic torque unit (Cybex II dynamometer). A separate apparatus was used to measure arm and leg capacities. Force exerted by the subject, measured as torque, was transferred from the dynamometer via an amplifier to a paper recorder and work integrator. Muscle strength was assessed with two individual maximal contractions for each muscle group at each of two contractile velocities, 36 and 180 degrees per second.

III. Results

The effect of virus inoculation on the test subjects is clearly illustrated in Figure 1. Rectal temperatures (T_{re}) began to increase 48 hrs after inoculation in the experimental subjects and reached their peak values within 72-96 hours after inoculation. No significant changes occurred in the T_{re} of the two controls. Experimental subjects developed the characteristic clinical findings and symptomatology for sandfly fever (Figure 2).

During the fever state, 3 subjects were unable to complete the submaximal treadmill walk.

Subject #4302 - felt dizzy at the end of 9% workload and the treadmill was stopped.

Subject #4307 - complained of shortness of breath, headache, and dizziness; treadmill stopped after 30 seconds at 12% grade.

Subject #4308 - stated that he could not complete test and stopped after 1.5 minutes at 9% grade.

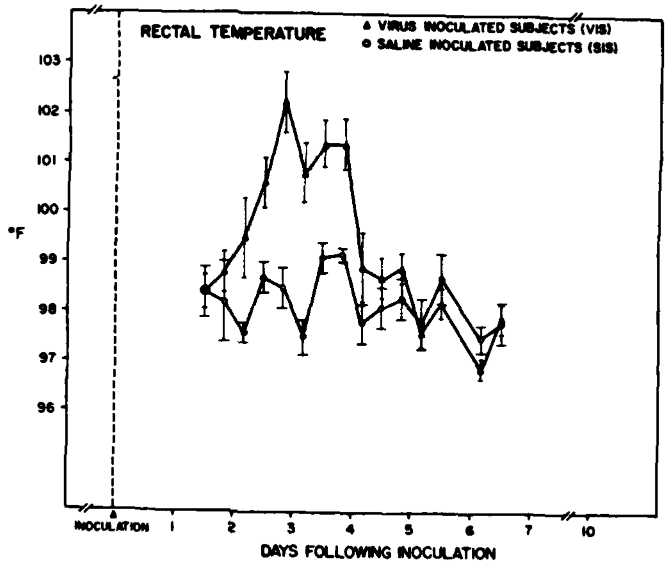

Figure 1. Effect of Sandfly Fever virus on rectal temperature.

During fever, the T_{re} was higher at all submaximal workloads as well as at rest. However, the rate at which T_{re} increased with exercise was not altered by the fever (Figure 3). Resting heart rate was also significantly elevated during fever. Exercise heart rates were also higher during fever than in either the pre or post fever state but the only significant difference was between the fever and post fever state at 0% grade (Figure 3).

The energy cost of walking was unaffected by the viral infection. Values obtained for oxygen consumption are listed in Table 2. Any differences between the values are within the limits of the measurement system or variations normally seen between subjects on repeated testing.

There were shifts in other parameters during fever that did indicate some effect due to viral infection. Perceived exertion (RPE)

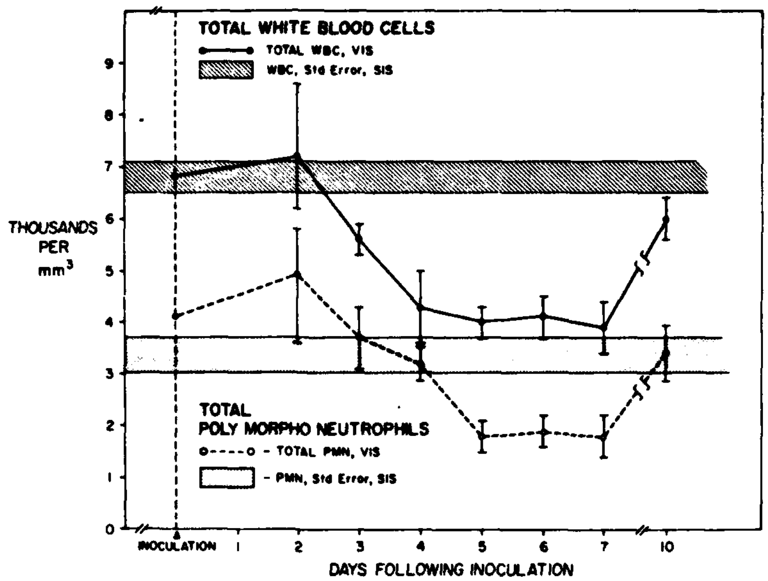

Figure 2. Effect of Sandfly Fever on total white cell count and polymorhoneutrophils.

(Borg's Scale) was significantly higher than the pre-inoculation values at 0% and 6% grade during the fever. Controls showed no change in RPE (Figure 4).

An increase in the ventilatory equivalent was also seen at the higher workloads in the experimental subjects (Figure 4). However, the control subjects also showed an increase in VEQ at higher workloads during the fever and post fever testing. Therefore, this increase could be due to some factor other than a direct effect of the virus.

In addition to the effects on submaximal walking performance, viral infection also caused a significant decrement on muscle strength measures. Mean strength capacities were reduced from 2 to 28% during fever. Values showed some signs of recovery during early convalescence but for the most part, they were still reduced. The control subjects were not affected in the same manner. The results of the muscle strength testing are summarized in Figure 5.

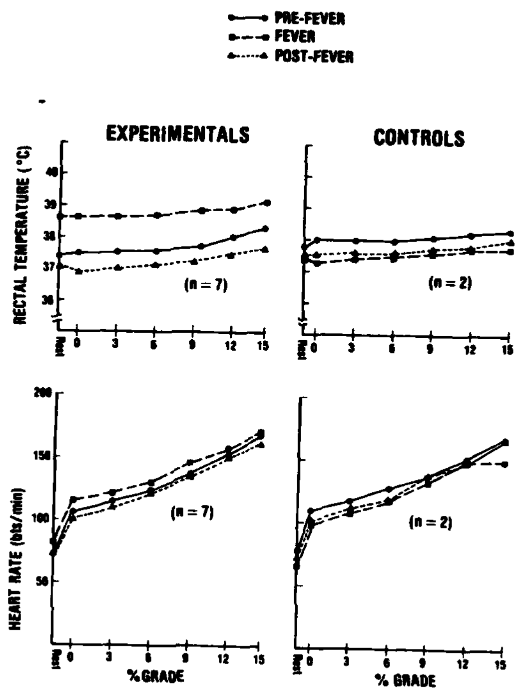

Figure 3. Comparisons of heart rate and rectal temperature during exercise.

All isometric tests were markedly decreased during fever. The decreases in upper torso, handgrip and leg isometric strength were all statistically signficant ($p < 0.05$). Although the overall effect of fever on back extensors and handgrip endurance was a decrease (15 and 28.6%, respectively), the effect was much more variable than in the other isometric measures and the decreases were not statistically significant. Dynamic strength was decreased only in the legs and this decrease was statistically significant only at the slow speed.

The final test results to be reported here are those obtained during the two maximal oxygen consumption determinations that the subjects performed. The results are summarized in Figure 6, which

Table 2. Oxygen consumption (ml/kg.min) while walking at increasing grade before, during and after fever.

	Pre-Inoculation	Fever	Convalescence
		3 mph 0%	
Experimentals (n = 6)	15.35	15.77	14.97
Controls (n = 2)	16.15	14.55	15.25
		3 mph 3%	
Experimentals	18.70	18.42	18.13
Controls	18.80	17.70	18.25
		3 mph 6%	
Experimentals	21.52	21.40	21.35
Controls	22.05	20.35	21.05
		3 mph 9%	
Experimentals	25.15	26.06	25.85
Controls	24.95	24.65	25.75
		3 mph 12%	
Experimentals	29.97	30.52(n=4)	29.32
Controls	30.45	29.30	30.25
		3 mph 15%	
Experimentals	35.15	33.70(n=4)	33.68
Controls	34.75	28.80(n=1)	34.40

illustrates that in all the parameters measured the response of the experimental subjects during early convalescence was lower than that of the controls. Generally the responses of the controls and experimentals were similar when compared to pre-fever values. Experimentals had slightly larger decreases in $\dot{V}O_2max$ and HR_{max}. Ventilation increased more in controls than the experimentals. The major difference between controls and experimentals was the grade at which they were working when they achieved maximum effort.

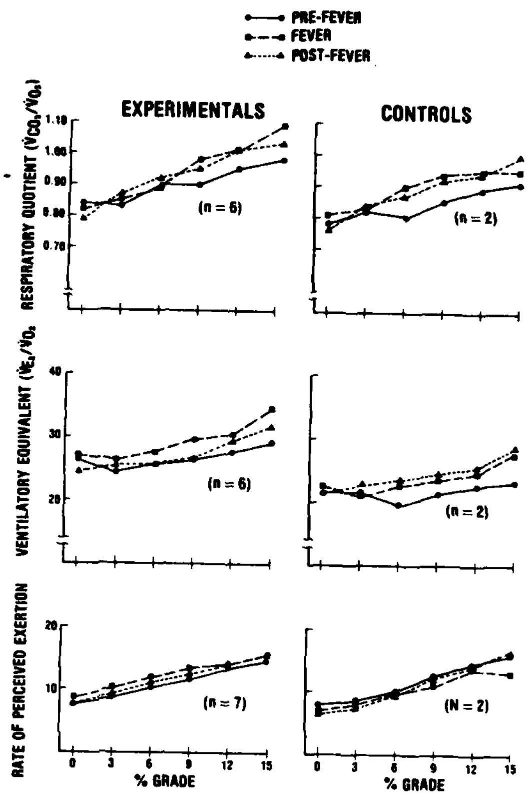

Figure 4. Comparison of respiratory quotient, ventilatory equivalent, and perceived exertion during exercise.

IV. Discussion

The results of this study indicate that in respect to physical performance, an acute viral infection shows the most detrimental effects on measures of muscle strength. These were especially apparent during the fever state. Although strength measures were still reduced during early convalescence, the reductions were not statistically significant. It is interesting to note that maximal isometric strength contractions appeared to be more affected than dynamic strength.

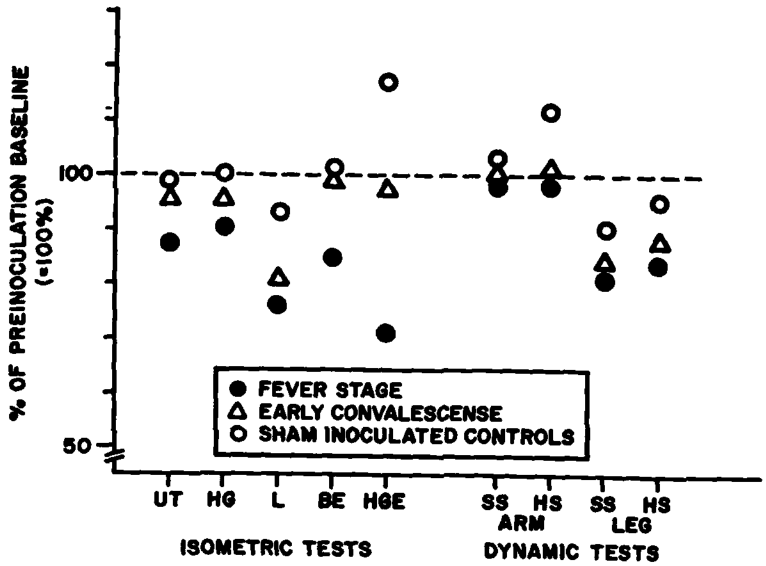

Figure 5. Comparison of muscle performance tests during Sandfly Fever Study.

The results obtained in this study agree very nicely with previous studies (4) which indicate that infectious disease has a detrimental effect on isometric muscle strength. The exact mechanism by which this occurs is not known. Muscle biopsies which were taken in this study indicate that a certain amount of protein breakdown occurs during viral infection. However, effects of virus upon the central and peripheral nervous system and upon the neuromuscular junction cannot be ruled out. The fact that isometric strength is affected more than dynamic strength may indicate that the viral infection interferes with the recruitment of muscle fibers during maximal contractions rather than having a direct effect on the muscle cells.

The submaximal walking data showed very few physiological differences between the various stages. Heart rate was elevated during the fever but this was only significant at the lower levels of exercise. This seems to indicate that the sympathetic drive which was present at rest during fever did not have an additive effect upon

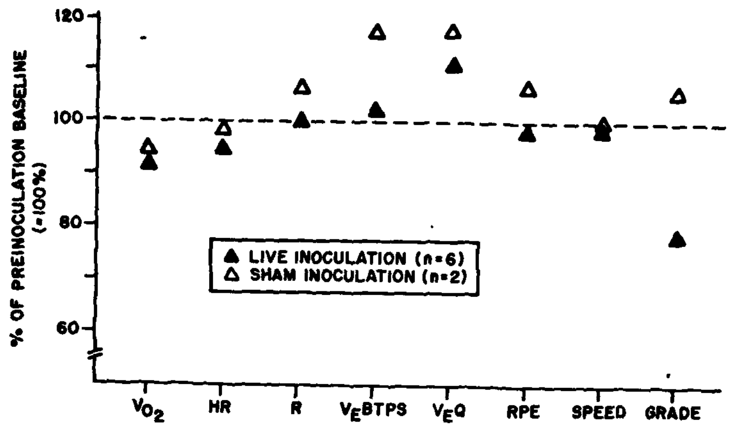

Figure 6. Data collected at $\dot{V}O_2$max prior to fever compared to early convalescence.

the sympathetic response to exercise at the higher workloads. It is also important to note that the rate of temperature increase during exercise was not altered during the fever state even though the T_{re} were almost 1°C higher during the fever stage. Elevated temperature also did not affect oxygen consumption. The most apparent effect of the virus on submaximal walking was the inability of three subjects to complete the task. However, there was no parameter that we measured which predicted this. The most striking relationship occurred between the subject's performance and his own rating of 4 specified symptoms (headache, myalgia, nausea and chills). The greater the sum of these symptoms; i.e., the sicker the individual felt; the worse his performance. Therefore, the virus appears to have a very marked effect upon the ability and/or the willingness of various individuals to perform work, moreso than an actual decrement in capacity.

Finally, in terms of aerobic capacity ($\dot{V}O_2max$), both the experimental and control subjects responded with a decrease in $\dot{V}O_2max$. It therefore appears that some other factor, other than the virus, was responsible. It is well known that bedrest or inactivity can cause significant decreases in aerobic capacity (5). This may have been a contributing factor in the decrease seen here. Another factor that may have influenced aerobic capacity was a loss of blood volume by the subjects. During this study a number of blood samples were obtained over the two week period in order to perform various laboratory and clinical tests. Although the amount taken at any one time was not large, the cumulative total was over 1.5 units of blood. It has also been demonstrated that if this amount of blood is removed at any single time, there will be a decrease in aerobic power (6). Therefore, it seems logical that this may also be a contributing factor to the decrease. There was one result, however, which also indicates that the virus is not without affect. Experimental subjects showed a marked decrease in the grade at which they achieved their maximum effort after the fever. This was in marked contrast to what was seen for the control subjects. This seems to indicate that the virus has some effect but just exactly what the mechanism involved would be, is not known.

In conclusion, the results of this study demonstrated quite clearly that an acute viral infection can have detrimental effects upon the individual's physical performance. Muscle strength and ability to perform submaximal work were clearly affected during the fever stage. Muscle strength and maximal aerobic power were still reduced in early convalescence although factors other than the infection may be responsible for the decrease in aerobic power. The effect of analgesic and anti-pyretic agents upon the symptoms of this viral infection were not looked at in this study. How the alleviation of symptoms would affect performance and muscle strength can only be determined by future study. However, commanders can expect that individuals suffering from acute viral infections will be unable to perform up to their potential capacity, not only during the infection, but also for at least a few days following the infection.

References

1. Bellanti, J.A., R.I. Krasner, P.J. Bartelloni, M.C. Young and W.R. Beisel. Sanfly fever: Sequential Changes in Neutrophil Biochemical and Bactericidal Functions. J. of Immunol. 108: 142-151, 1972.

2. Borg, G. and B.J. Noble. Perceived Exertion. In: Exercise and Sports Sciences Reviews, J.H. Wilmore (ed.). New York, Academic Press. pp. 131-153, 1974.

3. Knapik, J.J., D.M. Kowal, P. Riley, J.E. Wright and M. Sacco. Development and Description of a Device for Static Measurement in Armed Forces Examination and Entrance Station. USARIEM Technical Report T-2/79, 1979.

4. Friman, G. Effect of Acute Infectious Disease on Human Isometric Muscle Endurance. Upsala J. Med. Sci. 83:105-108, 1978.

5. Friman, G. Effect of Clinical Bed Rest for Seven Days on Physical Performance. Acta Med. Scand. 205:389-393, 1979.

6. Ekblom, B., A.N. Goldborg and B. Gullbring. Response to exercise after blood loss and reinfusion. J. Appl. Physiol. 33(2)175-180, 1972.